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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/585,420

08/28/2006

Braj Bhushan Lohray

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EXAMINER

SEAMAN, D MARGARET M

ART UNIT

PAPER NUMBER

1625

MAIL DATE

DELIVERY MODE

01/05/2010

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/585,420	Applicant(s) LOHRAY ET AL.	
	Examiner D. Margaret Seaman	Art Unit 1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-12 is/are pending in the application.
 4a) Of the above claim(s) 1 is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 2-12 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. ____.
 3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____. |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>7/7/06</u> . | 6) <input type="checkbox"/> Other: ____. |

DETAILED ACTION

Claim Objections

1. Claims 1-12 are objected to because of the following informalities: There was a preliminary amendment to the claims dated 7/7/2006 that deleted claim 1 and amended other claims. The new set of claims entered 2/23/2009 do not contain these amendments of the preliminary amendment of 7/7/2006. Due to this amendment (new set of claims), the most current set of claims is the claim set dated 2/23/2009, but it is improper since it does not include the amendments of 7/7/2006. It is suggested that these amendments be re-entered in response to this office action. This office action will be worked from the set of claims resulting from the preliminary amendment dated 7/7/2006. Appropriate correction is required. Claim 1 is deleted. Claims 2-12 are before the Examiner.

Claim Rejections - 35 USC § 101

2. 35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

3. Claim 9 is rejected under 35 U.S.C. § 101 because the claimed invention is directed to non-statutory subject matter, i.e. "Use of" is not a statutory subject matter; however, "A method of using..." is proper statutory subject matter.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

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The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claim 12 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while maybe enabling for making salts of the claimed compounds, does not reasonably provide enablement for making solvates of the claimed compounds. The specification does not enable any person skilled in the art of synthetic organic chemistry to make the invention commensurate in scope with these claims. “The factors to be considered [in making an enablement rejection] have been summarized as a) the quantity of experimentation necessary, b) the amount of guidance or direction presented, c) the presence or absence of working examples, d) the nature of the invention, e) the state of the prior art, f) the relative skill of those in that art, g) the predictability or unpredictability of the art, h) and the breadth of the claims”, *In re Rainer*, 146 USPQ 218 (1965); *In re Colianni*, 195 USPQ 150, *Ex parte Formal*, 230 USPQ 546. In the present case, the important factors leading to a conclusion of undue experimentation are c) the absence of any working example of a formed solvate, the lack of predictability in the art, and the broad scope of the claims. There are no working examples of any solvate formed. The claims are drawn to solvates, yet the numerous examples presented all fail to produce a single solvate. These cannot be simply willed into existence. As was stated in *Morton International Inc. v. Cardinal Chemical Co*, 28 USPQ2d 1190 “The specification purports to teach, with over fifty examples, the preparation of the claimed compounds with the required connectivity. However...there is no evidence that such compounds exist...the examples of the ‘881 patent do not produce the postulated compounds...there is ... no evidence that such compounds even exist.” The same circumstances appear to be true here. There is no evidence that solvates of the

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instantly claimed compounds actually exist; if they did, they would have been formed. Hence, applicants must show that solvates can be made, or limit the claims accordingly. G) The state of the art is that it is not predictable whether solvates will form or what their composition will be. In the language of the physical chemist, a solvate of an organic molecule is an interstitial solid solution. This phrase is defined in the second paragraph on page 358 of West (Solid State Chemistry). West, Anthony R., "Solid State Chemistry and its Application, Wiley, New York, 1988, pages 358 & 365. The solvent molecule is a species introduced into the crystal and not part of the organic host molecule is left out or replaced. In the first paragraph on page 365, West says, "it is not usually possible to predict whether solid solution will form, or if they do form, what is their compositional extent". Thus, in the absence of experimentation, one cannot predict if a particular solvent will solvate any particular crystal. One cannot predict the stoichiometry of the formed solvate, i.e. if one, two or a half of a molecule of solvent added per molecule of host. In the same paragraph on page 365, West explains that it is possible to make meta-stable non-equilibrium solvates, further clouding what Applicants mean by the word solvate. Compared with polymorphs, there is an additional degree of freedom to solvates, which means a different solvent or even the moisture of the air that might change the stable region of the solvate. H) The breadth of the claims includes all of the hundreds of thousands of compounds of formula (I) as well as the presently unknown list of solvents embraced by the term "solvate. Thus, the scope is broad.

6. Claim 8 is rejected under 35 U.S.C. 112, 1st paragraph, because the specification, while possibly being enabling for treating specific diseases, does not reasonably provide enablement

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for preventing diseases. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. Applicants are not enabled for preventing any of these diseases. The only established prophylactics are vaccines not the compounds such as presently claimed. In addition, it is presumed that “prevention” of the claimed diseases would require a method of identifying those individuals who will develop the claimed diseases before they exhibit the symptoms.

There is no evidence of record that would guide the skilled clinician to identify those who have the potential of becoming afflicted. “The factors to be considered [in making an enablement rejection] have been summarized as a) the quantity of experimentation necessary, b) the amount of direction or guidance presented, c) the presence or absence of working examples, d) the nature of the invention, e) the state of the prior art, f) the relative skill of those in that art, g) the predictability or unpredictability of the art, h) and the breadth of the claims”, *In re Rainer*, 146 USPQ 218 (1965); *In re Colianni*, 195 USPQ 150, *Ex parte Formal*, 230 USPQ 546. a) As discussed above, preventing diseases required identifying those patients who will acquire the disease before the disease occurs. This would require extensive and potentially open-ended clinical research on healthy subjects. B) The passage spanning lines of the instant specification, lists the diseases applicant intends to prevent. C) There are no working examples of such preventive procedure in a man or animal in the specification. D) The claims rejected are drawn to the medical prevention and are therefore physiological in nature. E) The state of the art is that no general procedure is art-recognized for determining which patients generally will become afflicted with disease before the fact. F) The artisan using Applicant’s invention would be a board certified physician who specializes in treating diseases. Despite intensive efforts,

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pharmaceutical science has been unable to find a way of getting a compound to be effective for the prevention of diseases generally. Under such circumstances, it is proper for the PTO to require evidence that such an unprecedented feat has actually been accomplished, *In re Ferens*, 163 USPQ 609. No such evidence has been presented in this case. The failure of skilled scientists to achieve a goal is substantial evidence that achieving such a goal is beyond the skill of the practitioners in that art, *Genetech vs. Novo Nordisk*, 42 USPQ2d 1001, 1006. This establishes that it is not reasonable to any agent to be able to prevent diseases generally. That is, the skill is so low that no compound effective generally against diseases has ever been found let alone one that can prevent such conditions. G) It is well established that “the scope of enablement varies inversely with the degree of unpredictability of the factors involved”, and physiological activity is generally considered to be an unpredictable factor. See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 214 (CCPA 1970). H) The claims broadly read on all patients, not just those undergoing therapy for the claimed diseases and on the multitude of compounds embraced by formula (I).

The Examiner suggests deletion of the word “prevention”.

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 2 and 11 are rejected under 35 U.S.C. 112, second paragraph, as failing to set forth the subject matter which applicant(s) regard as their invention. Claim 11 is unclear because it is missing the “.” Period at the end of the claim. Claim 2 is unclear due to the bounds of the “Z” moiety are outside those set in claim 12 from which it depends. Correction is required.

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Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

4. Claims 2-12 are rejected under 35 U.S.C. 102(e) as being anticipated by Beyer (US Patent 7138264, 7529628) and Magnus (US Patent 6770763). Beyer teaches compounds such as

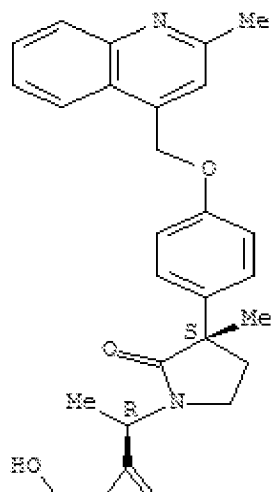
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RN 478911-60-3 CA

CN 1-Pyrrolidineacetamida, N-hydroxy- α ,3-dimethyl-3-[4-[(2-methyl-4-quinolinyl)methoxy]phenyl]-2-oxo-, (3R,3S)- (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A

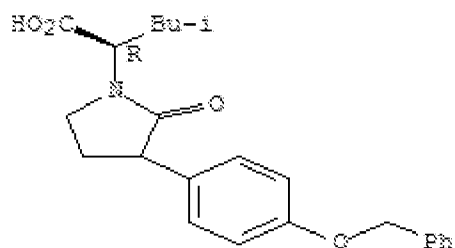


that anticipate the instant claims. Magnus teaches compounds such as

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RN 004130-00-4 CA
 CN 1-Pyrrolidineacetic acid, α -(2-methylpropyl)-2-oxo-3-[4-(phenylmethoxy)phenyl]-, (α R)- (CA INDEX NAME)

Absolute stereochemistry.



that anticipate the

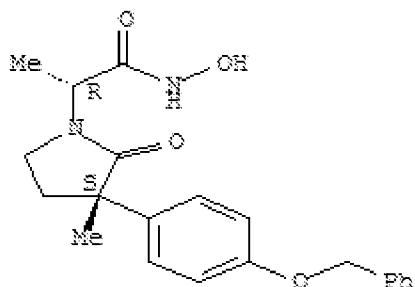
instant claims.

5. Claims 2-12 are rejected under 35 U.S.C. 102(b) as being anticipated by Wassermann and Duan (US PGPub 20030225054).

Wassermann teaches compounds such as

RN 223406-03-9 CA
 CN 1-Pyrrolidineacetamide, N-hydroxy- α ,3-dimethyl-2-oxo-3-[4-(phenylmethoxy)phenyl]-, (α R,3S)- (CA INDEX NAME)

Absolute stereochemistry.



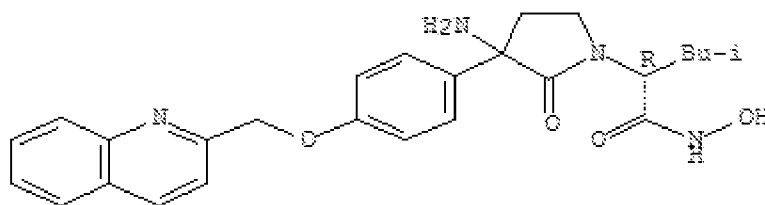
tha

t anticipate the instant claims. Duan teaches compounds such as

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RN 228402-98-0 CA
CN 1-Pyrrolidineacetamide, 3-amino-N-hydroxy- α -(2-methylpropyl)-2-oxo-3-[4-(2-quinolinyloxy)phenyl]-, (S)- (CA INDEX NAME)

Absolute stereochemistry.



that anticipates the instant claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to D. Margaret Seaman whose telephone number is 571-272-0694. The examiner can normally be reached on 730am-4pm, Monday-Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on 571-272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

D. Margaret Seaman
Primary Examiner
Art Unit 1625

/D. Margaret Seaman/
Primary Examiner, Art Unit 1625

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